



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN 31 2007

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Secondary Review of Oak Ridge National Laboratory's Evaluation of Submissions to Register WEED WORKS WEED & GRASS KILLER by Organic Works, Inc. (EPA File Symbol 81936-R): Product Chemistry Data; OPPTS 860 Series, Acute Toxicity and Non-Target Organism Data Waiver Requests

FROM: Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory

THROUGH: Carol E. Frazer, Ph.D., Toxicologist *Carol*
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511P)

TO: Todd Peterson, Ph.D., Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511P)

SUBMISSION CONTENTS:

1. WEED WORKS Weed and Grass Killer (EPA File Symbol 81936-R) product chemistry (OPPTS 880 and 830 series) (MRID 469583-01), OPPTS 860 series waiver request (MRID 469441-03), Tier I acute toxicity data waiver request (MRID 469441-02), Non-target organism toxicity data waiver request (MRID 469411-04) and Supplemental material for waivers (MRID 469441-05) (Chemical No. 044001; DP# 334682; D#370953; S800225)
2. Product contents: 20% acetic acid and 80% other ingredients

ACTION REQUESTED:

On September 15, 2006, Frederick D. Obenchain, Ph.D., Regulatory Affairs Agent of BioNet International Corp., Agents for Organic Works, Inc., submitted material to support the

registration of WEED WORKS Weed & Grass Killer (EPA Reg. Symbol 81936-R) with 20% acetic acid as the active ingredient. This included product chemistry and several waiver requests.

CONCLUSIONS:

All the waiver requests are ACCEPTABLE, but there are several problems with product chemistry which are UNACCEPTABLE, but UPGRADEABLE:

- Production process quantitative details must be provided. How much of each ingredient is used, how long and at what temperature the various steps are;
- The CSF is confusing regarding the TGAI – it is 20.00% of the EP, not 100%. This is not a formulation but an integrated production – the active ingredient is not registered. The CSF should remove the statement “=100% formulation;”
- Minor components on the CSF resulting from formulation should be listed as “impurities” in column 15;
- The inert ingredient [REDACTED] does not have the CAS number on CSF List #10, nor is #11 filled out with the Supplier name and address. If this is simply the [REDACTED] please list name and address. Total Weight (Item #17) is not filled out;
- Also, viscosity of the product is missing and the registrant should ensure the one-year storage stability and corrosion characteristics studies are submitted upon completion.

DATA EVALUATION RECORD

ACETIC ACID (Weed Works Weed & Grass Killer)

STUDY TYPE: Waiver Request for Tier I Acute Toxicity Studies

DATA EVALUATION RECORD

EPA Secondary Reviewer: Carol E. Frazer, Ph.D.

STUDY TYPE:	Waiver Requests for Acute Oral Toxicity (OPPTS 870.1100), Acute Dermal Toxicity (OPPTS 870.1200), Acute Inhalation Toxicity (OPPTS 870.1300), Acute Eye Irritation (OPPTS 870.2400), Acute Dermal Irritation (OPPTS 870.2500), Skin Sensitization (OPPTS 870.2600), Hypersensitivity Incidents, Bacterial Reverse Mutation Testing (OPPTS 870.5100), Continuous Inhalation Testing (OPPTS 870.3100-3465 series), Prenatal Developmental Toxicity Testing (OPPTS 870.3700)
MRID NO:	46944102
DP BARCODE:	DP334682
DECISION NO:	370953
SUBMISSION NO:	Not provided
TEST MATERIAL:	Weed Works Weed & Grass Killer (a.i., 20% w/w acetic acid)
STUDY NO:	Tier I Tox. Review. 2006. Reg. Support
SPONSOR:	Organic Works, Inc., 2023 E. Sims Way, Suite 358, Port Townsend, WA 98368
TESTING FACILITY:	N/A
TITLE OF REPORT:	Review of Tier I Acute Toxicity Studies Supporting the U.S. E.P.A. Registration of "Weed Works Weed & Grass Killer"
AUTHOR:	Obenchain, F.D.
STUDY COMPLETED:	September 11, 2006
CONFIDENTIALITY	None

CLAIMS:

GOOD LABORATORY PRACTICE:

A signed and dated GLP statement was provided. The submitter was neither the sponsor of the studies nor conducted them, and cannot confirm that the studies were conducted in compliance with 40 CFR Part 160.

CONCLUSION:

The information submitted is adequate to support the requested waivers for acute toxicity testing.

Test Material

Weed Works Weed & Grass Killer (a.i., 20% w/w acetic acid)

Product Description

Weed Works Weed & Grass Killer is an end use product intended to be used for non-selective control of herbaceous broadleaf weeds and weed grasses on non-crop, right-of-way, and industrial land sites.

Waiver Request

The registrant is requesting a waiver from the following data requirements:

Acute Oral Toxicity	OPPTS 870.1100
Acute Dermal Toxicity	OPPTS 870.1200
Acute Inhalation Toxicity	OPPTS 870.1300
Acute Eye Irritation	OPPTS 870.2400
Acute Dermal Irritation	OPPTS 870.2500
Skin Sensitization	OPPTS 870.2600
Hypersensitivity Incidents	
Bacterial Reverse Mutation Testing	OPPTS 870.5100
Continuous Inhalation Testing	OPPTS 870.3100-3465 series
Prenatal Developmental Toxicity Testing	OPPTS 870.3700

Registrant's Justification

The active ingredient in Weed Works Weed & Grass Killer is acetic acid, which is supplied by food-grade distilled white vinegar without any further dilution or adulteration. Impurities in the product potentially present at >0.1% w/w are [REDACTED] which preliminary assay determined are present at [REDACTED] respectively. Both [REDACTED] are GRAS and are present in food at substantially higher levels than in the end use product. [REDACTED] a Category 3 carcinogen, is present in the product at [REDACTED] which is less than

[REDACTED] The inert ingredient in the product is [REDACTED]

The HPV Chemical Challenge Program has concluded that no additional mammalian toxicity testing is necessary for the chemical category of acetic acid and its salts (MRID 46944105).

Acute Oral Toxicity

The acute oral LD₅₀ for acetic acid in rats is 3310 mg/kg (Comm. on Physical Sci., Math., and Appl., 1995, attached to MRID 46941102). In mice, an LD₅₀ of 4960 mg/kg is reported (Woodward et al., 1941, cited by HPV, 2001). The lowest reported lethal dose in humans as 308 mg/kg (Comm. on Physical Sci., Math., and Appl., 1995).

Acute Dermal Toxicity

An acute dermal LD₅₀ of 1060 mg/kg was reported for acetic acid in rabbits (Union Carbide Corp. Data Sheet, 1963, cited by HPV, 2001).

Acute Inhalation Toxicity

Inhalation toxicity values for acetic acid found in the public literature were an LC₅₀ of 5620 ppm/hr for mice (Chiringhelli and Difabio, 1957, cited by HPV, 2001), and an LC₅₀ of 11.4 mg/L for rats (BASF, 1989, cited by HPV, 2001). The lowest published toxic concentration by human inhalation is 816 ppm/m³ (Oxford Univ., 2006, attached to MRID 46941102).

Acute Eye Irritation

In an open irritation test to the eye of rabbits, acetic acid (no concentration provided) was reported to produce severe irritation effects (Oxford Univ., 2006). No other citable study was located. The registrant requests a waiver from any additional eye irritation studies based on the corrosive properties of acetic acid when applied to the eyes of suitable animal model systems. The reviewer notes that the appropriate warning is provided on the proposed product label.

Acute Dermal Irritation

Acetic acid (no concentration provided) was reported to produce severe irritation effects following open administration to rabbit skin and mild irritation effects following open administration of 50 mg for 24 hours to human skin (Oxford Univ., 2006). No other citable study was located. The registrant requests a waiver from any additional skin irritation studies based on the corrosive properties of acetic acid when applied to the skin of suitable animal model systems.

Skin Sensitization

No studies for skin sensitization by acetic acid were located in the literature. The registrant requests a waiver from any additional skin sensitization studies based on the corrosive properties of acetic acid when applied to the skin of suitable animal model systems. The registrant is not aware of any hypersensitivity incidents, but any incidents will be immediately reported to the Agency whenever the registrant becomes aware of them.

Bacterial Reverse Mutation

Three Ames tests using acetic acid, one a GLP study, were cited by the HPV Chemical Challenge Program (MRID 46944105). All the tests found no genotoxic effects with or without metabolic activation.

Continuous Inhalation

The NIOSH Recommended Exposure Limits for acetic acid in the workplace are a time-weighted average of 10 ppm (25 mg/m³), with a short term exposure limit of 15 ppm (37 mg/m³) (NIOSH, 2005). The OSHA Permissible Exposure Limit is a TWA of 10 ppm (25 mg/m³). In a rat study cited by the HPV Chemical Challenge Program (MRID 46944105), continuous inhalation of 11 to 35 ppm acetic acid for 3 to 35 days decreased activity, produced behavioral changes, and reduced work capacity. This registrant recognizes that this study does not meet OPPTS guideline requirements for a 90-day exposure period, but, based on the relatively low volatility of acetic acid and existing regulations for worker exposure, requests a waiver for any additional continuous inhalation studies.

Teratogenicity

The HPV Chemical Challenge Program (MRID 46944105) cites three studies for acetic acid in the form of 5% table strength apple cider vinegar. In mice receiving doses up to 1600 mg/kg/day for 17 days, no effects on nidation or on maternal or fetal survival were reported. In rats receiving doses up to 1600 mg/kg/day for 10 days, no effects on nidation or on maternal or fetal survival were reported. In rabbits receiving doses up to 1600 mg/kg/day for 23 days, no effects on nidation or on maternal or fetal survival were reported.

Reviewer's Conclusion

The reviewer concludes the information provided is sufficient to support the requested acute toxicity testing waivers.

Literature Cited

Comm. on Physical Sci., Math., and Appl. 1995. Prudent Practices in the Laboratory: Handling and Disposal of Chemicals – Lab Chem. Safety Summary: Acetic Acid. Nat. Acad. Press.

NIOSH. 2005. NIOSH Pocket Guide to Chemical Hazards – Acetic Acid. CDC Website.

Oxford Univ. 2006. MSDS for Acetic Acid. Oxford University Homepage.

U.S. High Production Volume (HPV) Chemical Challenge Program. 2001. Robust Summaries for Acetic Acid and Salts Category. Submitted as MRID 46944105.

DATA EVALUATION RECORD

ACETIC ACID (Weed Works Weed & Grass Killer)

STUDY TYPE: Waiver Request for Non-Target Organism Toxicity Studies

DATA EVALUATION RECORD

EPA Secondary Reviewer: Carol E. Frazer, Ph.D.

STUDY TYPE:	Waiver Requests for Avian Acute Oral Toxicity (OPPTS 850.2100), Avian Dietary Toxicity (OPPTS 850.2200), Freshwater Fish Toxicity (OPPTS 850.1075), Freshwater Invertebrate Toxicity (OPPTS 850.1010), Nontarget Plant Studies (OPPTS 850.4000), Nontarget Insect Testing (OPPTS 850.2500)
MRID NO:	46944104
DP BARCODE:	DP334682
DECISION NO:	370953
SUBMISSION NO:	Not provided
TEST MATERIAL:	Weed Works Weed & Grass Killer (a.i., 20% w/w acetic acid)
STUDY NO:	Tier I Tox. Review. 2006. Reg. Support
SPONSOR:	Organic Works, Inc., 2023 E. Sims Way, Suite 358, Port Townsend, WA 98368
TESTING FACILITY:	N/A
TITLE OF REPORT:	Review of Biochemical Pesticide Nontarget Organisms & Environmental Expression Data Supporting the U.S. E.P.A. Registration of "WeedWorks Weed & Grass Killer"
AUTHOR:	Obenchain, F.D.
STUDY COMPLETED:	September 11, 2006
CONFIDENTIALITY CLAIMS:	None

**GOOD LABORATORY
PRACTICE:**

A signed and dated GLP statement was provided. The submitter was neither the sponsor of the studies nor conducted them, and cannot confirm that the studies were conducted in compliance with 40 CFR Part 160.

CONCLUSION:

The information submitted is sufficient to support the requested waivers for avian acute oral toxicity and avian dietary toxicity, freshwater fish toxicity, freshwater invertebrate toxicity, and nontarget plant studies. The information provided does not support the requested waiver for nontarget insect testing.

Test Material

Weed Works Weed & Grass Killer (a.i., 20% w/w acetic acid)

Product Description

Weed Works Weed & Grass Killer is an end use product intended to be used for non-selective control of herbaceous broadleaf weeds and weed grasses on non-crop, right-of-way, and industrial land sites.

Waiver Request

The registrant is requesting a waiver from the following data requirements:

Avian Acute Oral Toxicity	(OPPTS 850.2100)
Avian Dietary Toxicity	(OPPTS 850.2200)
Freshwater Fish Toxicity	(OPPTS 850.1075)
Freshwater Invertebrate Toxicity	(OPPTS 850.1010)
Nontarget Plant Studies	(OPPTS 850.4000)
Nontarget Insect Testing	(OPPTS 850.2500)

Registrant's Justification

The active ingredient in the product is acetic acid, supplied by food-grade distilled white vinegar without any further dilution or adulteration. Impurities in the product potentially present at [REDACTED] which preliminary assay determined are present at [REDACTED] respectively. Both [REDACTED] are present in food at substantially higher levels than in the product and are GRAS. [REDACTED] a Category 3 carcinogen, is present in the product at [REDACTED] which is less than [REDACTED]

The inert ingredient in the product is [REDACTED]

Avian Acute Oral Toxicity, Avian Dietary Toxicity

No data were found regarding avian acute oral toxicity. The registrant attributes the lack of data to a) the low toxicity of acetic acid and its salts to mammals (see MRID 46944102); b) the unlikely exposure of birds to dietary acetic acid due to its rapid partition into the water (73%) and air (~27%) components of the environment; c) its rapid biodegradation and photodegradation; and d) the ubiquity of its use as a food additive. The registrant notes that the product label states "Do not apply to roosting or nesting birds,"

Freshwater Fish Toxicity

The HPV Chemical Challenge Program (2001) cites a 96-hr LC₅₀ of 75 mg/L for bluegill sunfish (*Lepomis macrochirus*), and a 96-hr LC₅₀ of 251 mg/L for mosquito fish (*Gambusia affinis*) (MRID 46944105). These data establish a low to moderate toxicity of acetic acid in natural environments. The product is not intended for use as an aquatic herbicide, and the label contains the following hazard statement: "Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment washwater or rinsate."

Freshwater Invertebrate Toxicity

The HPV Chemical Challenge Program (2001) cites a 24-hr LC₅₀ of 47 mg/L for *Daphnia magna* under static condition. In static studies with *Daphnia magna* using immobility as the endpoint, a 24 hour EC₅₀ of 6000 mg/L was determined for acetic acid solution neutralized to pH 8.0, and a 24-hr EC₅₀ of 95 mg/L was determined for acetic acid without neutralization, indicating the effect of acetic acid was strongly related to pH. In another static test using immobility as the endpoint, a 48-hr EC₅₀ of 65 mg/L was determined.

The product is not intended for use as an aquatic herbicide, and the label contains the following hazard statement: "Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment washwater or rinsate."

Nontarget Plant Studies

The product is a non-selective herbicide for non-crop terrestrial plants. The pH effect of acetic acid on terrestrial plants disrupts the cuticle on the plant leaf and stem surfaces, leading to rapid dessication. In the aquatic environment, dessication should not be expected. The HPV Chemical Challenge Program (2001) cites a toxicity threshold of 4000 mg/L for growth inhibition of the algae *Scenedesmus quadricauda* in an eight-day test.

Nontarget Insect Testing

No published data were found on the effects of acetic acid on honeybees or other nontarget insects. The proposed product label includes the following statement: "Do not apply to ... flowering plants during times of day when bees are actively foraging."

Reviewer's Conclusion

The reviewer concludes the information provided is sufficient to support the requested waivers for avian acute oral toxicity and avian dietary toxicity, freshwater fish toxicity, freshwater invertebrate toxicity, and nontarget plant studies. The information provided does not support the requested waiver for nontarget insect testing, and as the product label warns against application when honeybees may be foraging, it is likely that direct application of the product to other nontarget insects will also be protected.

Literature Cited

U.S. High Production Volume (HPV) Chemical Challenge Program. 2001. Robust Summaries for Acetic Acid and Salts Category. Submitted as MRID 46944105.